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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,104	08/17/2000	Walter Birchmeier	105357-427-NP	5225

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EXAMINER	
KAM, CHIH MIN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/641,104	BIRCHMEIER ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The Request for Continued Examination (RCE) filed March 12, 2004 under 37 CFR 1.114 is acknowledged. An action on the RCE follows.

Status of the Claims

2. Claims 44-50 are pending.

The previous amendment filed August 20, 2003 has been entered. Applicant's preliminary amendment filed March 12, 2004 is acknowledged, and applicants' response has been fully considered. Claims 1-41 have been cancelled. New claims 42-48 (applicants' numbering in the preliminary amendment) have been added, where the numbering of claims 42-48 have been changed to claims 44-50 according to 37 C.F.R. 1.126 because there were claims 42 and 43, which have been cancelled in the amendment filed August 20, 2003. Thus, claims 44-50 and SEQ ID NOs: 6, 7, 8, 9, 10, 11 and 12 are examined.

Objection Withdrawn

3. The previous objection to the specification is withdrawn in view of applicants' amendment to the specification in the amendments filed August 20, 2003 and March 12, 2004.

4. The previous objection to claims 39 and 43 is withdrawn in view of applicants' cancellation of the claim in the amendments filed August 20, 2003 and March 12, 2004.

Rejection Withdrawn

Claim Rejections - 35 USC § 112

5. The previous rejection of claims 39-43 under 35 USC § 112, first and second paragraphs, is withdrawn in view of applicants' cancellation of the claim in the amendments filed August 20, 2003 and March 12, 2004.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 44-50 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide from armadillo domains of β-catenin such as SEQ ID NOs: 6, 7, 8, 9, 10, 11 and 12 which inhibits the interaction between β-catenin and a transcription factor or a tumor suppressor protein; or specific mutants of these armadillo peptides of β-catenin (arms 3-8) which have residue(s) 253, 260, 274, 292, 338, 342, 345, 354, 383, 386, 394, 435, 457, 469 or 470 (numbering according to human β-catenin sequence) substituted by Ala, Val, Leu or Ile, does not reasonably provide enablement for a peptide from armadillo domains of β-catenin having SEQ ID NO: 6, 7, 8, 9, 10, 11 or 12 which enhances the interaction between β-catenin and a transcription factor or a tumor suppressor protein; or, an undefined mutant of a β-catenin armadillo peptide (arms 3-9) or of an armadillo domain of β-catenin polypeptide, which affects (e.g., inhibits or enhances) the interaction between β-catenin and a transcription factor or a tumor suppressor protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 44-50 encompass an armadillo peptide of β-catenin (arms 3-9; SEQ ID NOs: 6, 7, 8, 9, 10, 11 and 12) or a mutant thereof, or a mutant of an armadillo domain of β-catenin polypeptide, which affects the interaction between β-catenin and a transcription factor or a tumor suppressor. The specification, however, only discloses cursory conclusions (pages 1 and 3)

without data supporting the findings, which states that the invention relates to agents for treating human illness such as cancers based on the agents which can affect the interaction between β-catenin and transcription factors or tumor suppressor gene products, and these agents can be peptides derived from β-catenin. There are no indicia that the present application enables the full scope in view of armadillo peptides of β-catenin or mutants thereof as discussed in the stated rejection. The present application does not provide sufficient teachings on the mutants of armadillo peptides and their effect on the interaction between β-catenin and a transcription factor or a tumor suppressor. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breadth of the claims, the absence or presence of working examples, the state of the prior art and relative skill of those in the art, the predictability or unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breadth of the claims:

The breadth of the claims is broad and encompasses unspecified variants regarding the mutants of armadillo domain of β-catenin polypeptide, which are not adequately described or demonstrated in the specification.

(2). The absence or presence of working examples:

There are no working examples indicating the claimed variants except for the specific armadillo peptides of β-catenin (arms 3-9; SEQ ID NO:6-12) and the specific mutants of these armadillo peptides (e.g., Ala substituents at specific positions; Example 4, Table 2).

(3). The state of the prior art and relative skill of those in the art:

The related art (WO 98/42296) indicates compounds that interact with stabilized β-catenin or LEF can be identified through the determination of the binding regions of β-catenin or LEF by experimentation or molecular modeling, however, such compounds have not been specified. The general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the identification of various mutants of armadillo domain of β-catenin polypeptides and their effects on the interaction between β-catenin and a transcription factor or a tumor suppressor to be considered enabling for variants.

(4). Predictability or unpredictability of the art:

The claims encompass peptides comprising armadillo peptides of β-catenin or mutants thereof, which affect the interaction between β-catenin and a transcription factor or a tumor suppressor, however, the specification only indicates certain armadillo peptides of β-catenin and certain mutants of these armadillo peptides inhibit the interaction between β-catenin and a transcription factor a tumor suppressor protein, it has not provide sufficient teaching on the identities various mutants of armadillo domain of β-catenin polypeptides, which enhance the interaction, thus, the invention is unpredictable regarding the amino acid sequences of the armadillo peptides having enhancement effect on the interaction.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to armadillo peptides of β-catenin or mutants thereof which affect the interaction between β-catenin and a transcription factor or a tumor suppressor. The specification indicates some basic (Lys, Arg, His) or some aromatic amino acids in the armadillo

repeat units 3-9 of β-catenin can be mutated to Ala (pages 6-7; Fig. 5), which inhibit the interaction with LEF-1/TCF, APC, conductin or E-cadherin are identified (Figs 5 and 6; Table 2; pages 9-10). However, the specification has not identified any armadillo peptide of β-catenin or mutant thereof which enhances the interaction. Moreover, the specification has not shown any mutants with different amino acid substitution other than Ala or aliphatic residues can affect (inhibit or enhance) the interaction between β-catenin and a transcription factor or a tumor suppressor. There are no working examples indicating various mutants of armadillo peptides of β-catenin other than Ala substitution at specific positions can affect the interaction between β-catenin and a transcription factor or a tumor suppressor. Since the specification fails to provide sufficient teachings on β-catenin armadillo peptides or the mutants thereof which enhance the interaction, it is necessary to carry out further experimentation to assess the effects of various mutants of armadillo peptides of β-catenin on the interaction between β-catenin and a transcription factor or a tumor suppressor.

(6). Nature of the Invention

The scope of the claims encompasses various armadillo peptides of β-catenin, or mutants thereof which affect the interaction between β-catenin and a transcription factor or a tumor suppressor, however, the specification does not provide sufficient teaching on the identities of various mutants of armadillo peptides of β-catenin which affect the interaction. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, while the working example does not sufficiently demonstrate the claimed variants, the effects of the claimed variants are unpredictable, and the teaching in the specification are limited, therefore, it is necessary to have

additional guidance and to carry out further experimentation to assess the effects of various armadillo peptides of β-catenin and their mutants on the interaction between β-catenin and a transcription factor or a tumor suppressor.

In response, applicants indicate the specification discloses the armadillo domain of human β-catenin and the key amino acid positions that affect the interaction between β-catenin and a transcription factor or a tumor suppressor, and how to inhibit the interaction of β-catenin and a transcription factor or a tumor suppressor by mutation; the claims are directed to the mutants of the armadillo domain of human β-catenin polypeptide and the mutated peptides of arms 3-8 of human β-catenin polypeptide, which are fully disclosed in Example 4 and Fig. 6, and the peptide sequence of human β-catenin was known to the one skilled in the art, and the claims recite the specific positions of mutations based on the known peptide sequence of human β-catenin polypeptide; and because Ala and other aliphatic amino acids are classified in the same class having similar properties, thus not only the Ala substitution but also the mutation by other aliphatic amino acids substitution at specific positions are enabled by the invention (pages 6-7 of the response). Applicant's response has been considered, however, the argument is not fully persuasive because the specification only shows certain positions of the armadillo repeat units 3-9 of β-catenin are mutated to Ala, and these mutated armadillo peptides inhibit the interaction of β-catenin with a transcription factor or a tumor suppressor, it does not demonstrate numerous mutants of the armadillo domain of human β-catenin polypeptide affect (including inhibit or enhance) the interaction of β-catenin with a transcription factor or a tumor suppressor, which are encompassed by the claim. Since the specification fails to provide sufficient teachings on mutants of armadillo domain of β-catenin polypeptide which affect the interaction between β-

catenin and a transcription factor or a tumor suppressor as indicated in the section above, it is necessary to carry out further experimentation to assess the effects of various mutants of armadillo domains of β-catenin polypeptide on the interaction. Regarding aliphatic amino acid substitution in the β-catenin armadillo peptides, the argument is persuasive, thus they are enabled.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 44-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

8. Claims 44-50 are indefinite as to "said peptide or polypeptide is selected from a group consisting of peptides or polypeptides having the amino acid sequences shown in SEQ ID NO:6.....", or "said mutant is selected from a group consisting of mutants of the armadillo domain of human β-contenin polypeptide having...". Note that Markush group is cited in the claim, where closed language should be used, however, the claim recites "peptides or polypeptides having the amino acid sequences shown in SEQ ID NO:6...." or "mutants of the armadillo domain of human β-contenin polypeptide having....", which indicates many peptides or mutants are encompassed and is an open language. Claims 47-50 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

9. Claims 45-50 are indefinite because the claim recites amino acid position(s) in the sequence (e.g., SEQ ID NO:6 having a mutation in Phe in position 253) without reference to an amino acid sequence identified with "SEQ ID NO:". The amino acid sequence of SEQ ID NO:6, which contains 41 amino acids, does not have amino acid position 253, thus SEQ ID NO:6 is not the sequence used for numbering the position. Claims 47-50 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

10. Claim 50 is indefinite because of the use of the term "LEF-1", "TCF-1", or "APC". The cited term renders the claim indefinite, it is not clear what the term stands for. A fully spelled out word should be indicated.

Conclusion

11. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Christopher S. F. Low

CHRISTOPHER S. F. LOW
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Chih-Min Kam, Ph. D. CMK
Patent Examiner

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April 28, 2004